SURGICAL MANAGEMENT OF OSTEOGENIC SARCOMA OF THE LOWER LIMB

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SURVIVAL and surgical management of osteogenic sarcoma have dramatically improved during the last decade. In the past, radical amputation and disarticulation were the only established surgical treatments of malignant osteogenic sarcoma.[1,5,14] Recent accomplishments in chemotherapy, progress in the surgical techniques of en bloc resection, and advances in joint replacement have resulted in limb sparing procedures for this highly malignant bone tumor.[3,6] We shall compare the survival and function in ablated versus limb preserved patients with osteogenic sarcoma of the lower limb at Memorial Hospital.

MATERIALS AND METHODS

Between December 1977 and December 1981 74 consecutive patients (48 male and 26 female) with primary malignant osteogenic sarcoma of the lower extremity were treated at Memorial Hospital by a single orthopedic surgeon (JML). All the patients had a biopsy showing high grade malignant spindle cell sarcoma depositing osteoid. The locations of the tumors were as follows: proximal femur (2), femoral shaft (6), distal femur (38), proximal tibia (22), distal tibia (2), proximal fibula (2), distal fibula (1), and calcaneus (1). The median age was 16 and ranged from five to 62 years. The patients were staged according to the Surgical Staging of the Musculoskeletal Tumor Society.[2] There were two patients in Stage IIA, 53 in Stage IIB, and 19 in Stage III. These patients were surgically treated by either ablative surgery (51) or en bloc resection (23). The ablative surgical procedures utilized were hemipelvectomy (1), hip disarticulation (11), above knee amputation (34), knee disarticulation (2), and below knee amputation (3).

All patients had routine history, physical examination, and complete labora-

TABLE I. CAUSES OF ABLATIVE SURGERY IN 51 PATIENTS WITH OSTEOGENIC SARCOMA BY LOCATION OF THE LESION

	Femur	*Tibia*	*Fibula*	*Calcaneus*	*Total*	*%*
Tumor size	7	4			11	(22)
Pathologic fracture	9* **		1		10	(19)
Neurovascular involvement	4	5			9	(17)
Infected biopsy	1	4			5	(10)
Tumor location	3†	1		1	5	(10)
Age		4			4	(8)
Previous surgery	1	3‡			4	(8)
Unreliable patient		2			2	(4)
Palliation	1				1	(2)

*One patient with fracture of the femoral shaft was treated elsewhere with intramedullary fixation thus spilling tumor cells.
**Two patients who had pathologic fractures also had infected biopsies.
†One patient with a large tumor of the proximal femur underwent hemipelvectomy.
‡In addition to tumor spillage from previous surgery, one patient developed a pathologic fracture.

tory determinations. The extent of disease was assessed by standard anteroposterior and lateral roentgenograms of the involved bone, bone scan, gallium scan, computerized axial tomography of the involved area, standard posteroanterior and lateral roentgenograms of the chest, and chest tomography. Biplane arteriography of the area involved with tumor was performed. Upon completion of this exhaustive work-up, the feasibility of en bloc resection was determined. The classical criteria followed for en bloc resection were absence of involvement of the neurovascular bundle and skin with tumor and the possibility of preserving a cuff of normal tissue around the entire tumor. Other factors crucial in making that decision included: completion of patient growth, size and site of tumor, response to preoperative chemotherapy, occurrence of a pathologic fracture, previous surgery elsewhere, "contamination" of soft tissue with tumor cells, and infection of the biopsy site. Practically all cases had an associated soft tissue mass preoperatively and this certainly did not, in itself, contraindicate limb salvage. Pulmonary metastases were not necessarily a contraindication for limb salvage as long as the primary lesion and the lung metastases appeared surgically resectable.

Table I shows the indications of ablative surgery in 51 patients in association with the location of the primary tumor. Large sized tumors, the occurrence of pathologic fracture, and neurovascular involvement by tumor were the three leading indications. Other indications included an infected biopsy, the location of the tumor, age (during the first decade of life), previous surgery with contamination of the soft tissue with tumor cells, an unreliable patient, and palliation.

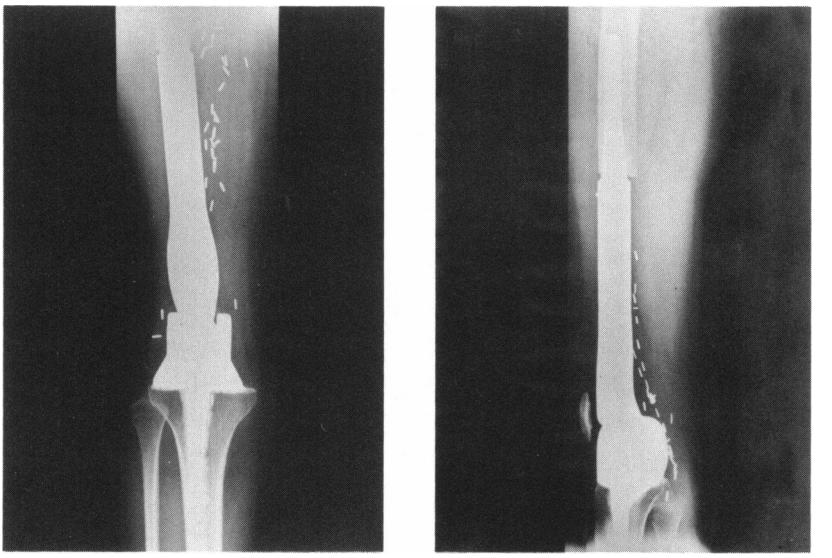

Fig. 1*a* and 2*b*. AP and lateral view of BL semiconstrained en bloc tumor prothesis inserted for a distal femoral osteogenic sarcoma.

In 13 patients with osteogenic sarcoma about the knee who were candidates for en bloc resections, leg length scanograms of both lower extremities were also obtained to create a custom-made total knee replacement developed at the Hospital for Special Surgery by Dr. Albert Burstein and Dr. Joseph Lane. The custom device is a semiconstrained titanium total knee that allows 5° of varus-valgus and rotatory motion. It is designed with a cementless fluted fixation stem proximally and a cementable tibial component distally (Figure 1).

The patients were initially started, following tissue biopsy, on a preoperative chemotherapy regimen of high dose methotrexate with citrovorum factor rescue in combination with either vincristine and adriamycin or bleomycin, cyclophosphamide, and dactinomycin.[11,12,13] Six to 12 weeks following preoperative chemotherapy, roentgenograms of the lesion, arteriogram, bone scan, and gallium scan were repeated to reassess the lesion. Depending on the above criteria, the patients had either ablative or en bloc resection of their tumor.

Table II describes the 23 patients who underwent en bloc resection. En bloc resections maintained a 5 to 10 cm intraosseous free margin beyond the tumor as determined by bone scan. This en bloc group was reconstructed with the custom made total knee replacement (13), total femur replacement (2), Van Ness turniplasty (4),[15] soft tissue reconstruction in two patients

TABLE II. LOWER EXTREMITIES SURVIVAL (NO EVIDENCE OF DISEASE)

	Stage II	*Stage III*
En Bloc	16/19 (84.2%)	1/4 (25%)
Ablative	31/36 (86.1%)	5/15 (33.3%)
Combined	47/55 (85.5%)*	6/19 (31.6%)

*$p < 0.0001$ (Chi square test)

with osteogenic sarcoma of the fibula, bipolar proximal femoral endoprosthetic hip replacement for proximal femoral lesion (1), and an intracallary allograft (1) for a lesion of the shaft of the femur. The remaining 51 patients did not meet criteria for en bloc resection (Table III). The ablative procedures performed included: hemipelvectomy (1), hip disarticulation (11), above knee amputation (34), knee disarticulation (2), and below knee amputation (3).

Histologic examination of all surgical specimens was performed. The degree of tumor destruction from chemotherapy was graded. The grading system used was developed at Memorial Sloan-Kettering Cancer Center by Dr. Huvos and defined complete tumor necrosis as Grade IV, more than 90% necrosis as Grade III, 50 to 90% necrosis as Grade II, less than 50% necrosis as Grade I.[3,4] Chemotherapy resumed two to three weeks postoperatively after adequate wound healing. Grade I and II responses required a change in chemotherapy to cis-platinum. Patients undergoing limb salvage procedures were protected with an ischial weight-bearing brace for six weeks to three months postoperatively then permitted to walk without braces. Patients who had amputations were fitted shortly after operation with a temporary pylon prosthesis for about one to two months until stump shrinkage ceased. Then they were fitted with a quadrilateral permanent prosthesis. All patients used either a cane or crutches to walk postoperatively and graduated in time to walking without aid.

Follow-up to death or last examination ranged from six to 64 months with a median follow-up from date of operation of 27 months for Stage II lesions and 21 months for Stage III lesions. In Stage II the median follow-up was 27 months for the en bloc group and 27 months for the amputated group. In Stage III the median follow-up was 22 months for the en bloc group and 21 months for the amputation group. All patients were followed postoperatively with serial chest radiographs and bone scans. Functional factors determined in the gait analysis laboratory at the Hospital for Special Surgery included stride length, velocity, oxygen consumption, and percent of maximum aerobic capacity at preferred walking and 20% augmented velocity.

TABLE III. SURVIVAL (74 PATIENTS)
(FROM TIME OF SURGERY TO 1/1/83)

		Femur			*Tibia*			
Stage	*Procedure*	*Proximal*	*Shaft*	*Distal*	*Proximal*	*Distal*	*Other*	*Overall*
II	En bloc resection	1/1	1/1	10/13 (76.9%)	2/2		2/2	16/19 (84.2%)
	Ablative surgery	1/1	3/3	10/15 (66.7%)	14/14	1/1	2/2	31/36 (86.1%)
III	En bloc resection			1/4 NED 1/4 AWD				1/4 NED (25%) 1/4 AWD (25%)
	Ablative surgery		1/2 NED	2/6 NED	2/6 NED 1/6 AWD	0/1 NED		5/15 NED (33.3%) 1/15 AWD (6.7%)

Numerator = number of alive patients
Denominator = total number of patients
NED = No evidence of disease, AWD = alive with disease

RESULTS

Patients with Stage IIA, IIB, and III high grade osteogenic sarcoma of the lower extremity were evaluated for survival and function following limb preserving en bloc resection or amputation. Most patients in all stages had lower extremity lesions located about the knee 62/74 (84%). Overall survival for osteogenic sarcoma differed, depending upon the stage of tumor: 47/55 (85.5%) patients with Stage II tumors (no distant metastases) have survived (NED) compared to 6/19 (31.6%) patients with Stage III disease (lung metastases) Tables IV, V, VI.

Within Stage II disease, both patients (2/2) with intraosseous disease (IIA) survived. The Stage IIB disease, extraosseous extension, has an overall survival of 45/53 (84.9%), and does not differ significantly from the limited number of patients with IIA disease. IIA disease represents a small fraction of this series and in fact is an uncommon stage of presentation (2/74 or 2.7% of total series). Due to similar survival, all IIA and IIB patients have been combined in the subsequent analysis.

Fifty-five patients with IIA and IIB stage osteogenic sarcomas had lesions of the distal femur or proximal tibia. Nineteen patients had limb preservation (35%) and 36 had amputations (65%). There was no significant difference between surgical treatment versus their survival within similar lesion sites; the distal femur (76.9% vs. 66.7%) or proximal tibia (100% vs. 100%) (Table VI). The improved survival for tibial lesions vs. distal femoral lesions was statistically significant ($p<0.02$, Chi square test). None of the Stage IIA or IIB en bloc resections were associated with local recurrences.

In terms of function (Table VII), the patients with limb preservation were statistically superior in overall gait and specifically velocity, stride length, oxygen consumption, and percentage of maximum aerobic capacity both at normal speed and 20% augmented velocity. The limb-preserved patient utilized less oxygen and less maximum aerobic capacity as compared to the amputation patient.

Patients presenting with Stage III osteogenic sarcoma (distant metastases) could be retrieved with combined local surgery and thoracotomies in the setting of appropriate chemotherapy. Only 4/19 patients underwent limb preservation. Within these limited numbers, 6/19 (32%) have no evidence of disease, 2/19 (11%) are alive with disease, and 11/19 (57%) are dead. The two patients currently alive with disease do not appear to be curable. Consequently, only 20% of the Stage III series appear at this early time to be potential long-term survivors. The survival of Stage III disease as compared

TABLE IV. VELOCITY AND OXYGEN CONSUMPTION

Controls	*Velocity* (M/Min)*	*Ml O_2 kg/m**	
		Free	*Fast*
(13)	61 ± 11	15 ± 1	15 ± 1
En blocs (08)	50 ± 10.5	25 ± 5	25 ± 5
Amputees (06)	41.6 ± 8.3	34 ± 3	34 ± 3
Control vs. En bloc	$p<0.05$	$p<0.01$	$p<0.01$
En bloc vs. Amputee	$p<0.05$	$p<0.01$	$p<0.01$

*Mean ± SD

TABLE V. LOWER EXTREMITIES SURVIVAL (NO EVIDENCE OF DISEASE)

	Stage II	*Stage III*
En Bloc	16/19 (84.2%)	1/4 (25%)
Ablative	31/36 (86.1%)	5/15 (33.3%)
Combined	47/55 (85.5%)*	6/19 (31.6%)

*$p<0.0001$ (Chi square test)

to Stage II disease is significantly inferior ($p<0.0001$), thus indicating a poor prognosis for patients presenting with lung metastases. There appeared to be no benefit for amputation over en bloc surgery in terms of overall survival. One en bloc patient had a delayed local recurrence in the form of massive lung metastases.

Patients undergoing en bloc procedures had a higher complication rate than those receiving amputation (Tables II, III) (12/23 en bloc versus 3/51 amputation). The most common problem was skin necrosis from nonviability of a skin flap. These required limited secondary skin procedures. The utilization of intraoperative intravenous vital dye (fluorescein) has permitted the surgeon to identify nonviable skin at the time of initial surgery and to debride it primarily at the time of closure. This technique has resulted in fewer skin complications recently. Two patients following infection (one in an allograft) and one patient with local recurrence (Stage III) required subsequent amputation.

DISCUSSION

A comprehensive analysis of 74 consecutive lower extremity osteogenic sarcomas clearly demonstrated that modern adjuvant chemotherapy both preoperative and postoperative coupled with appropriate surgical excision can lead to an 85%, 27 month survival rate without evidence of disease in patients presenting with localized tumors. Conversely, patients who pres-

TABLE VI. SURVIVAL (74 PATIENTS)
(FROM TIME OF SURGERY TO 1/1/83)

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II	En bloc resection	1/1	1/1	10/13 (76.9%)	2/2		2/2	16/19 (84.2%)
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	Ablative surgery		1/2 NED	2/6 NED	2/6 NED 1/6 AWD	0/1 NED		5/15 NED (33.3%) 1/15 AWD (6.7%)

Numerator = number of alive patients
Denominator = total number of patients
NED = No evidence of disease, AWD = alive with disease

TABLE VII. VELOCITY AND OXYGEN CONSUMPTION

Controls	*Velocity** *(M/Min)*	*Ml O_2 kg/m**	
		Free	*Fast*
(13)	61 ± 11	15 ± 1	15 ± 1
En blocs (08)	50 ± 10.5	25 ± 5	25 ± 5
Amputees (06)	41.6 ± 8.3	34 ± 3	34 ± 3
Control vs. En bloc	$p<0.05$	$p<0.01$	$p<0.01$
En bloc vs. Amputee	$p<0.05$	$p<0.01$	$p<0.01$

*Mean ± SD

ent with lung metastases in spite of thoracotomies, chemotherapy, and surgical excision of local tumor have a significantly lower survival rate (31%; $p<0.0001$). Limb preservation when properly chosen can provide survival rates comparable to amputations for similar staged and anatomically located tumors.

Within this series, proximal tibial lesions had a superior survival rate to distal femoral lesions (100% versus 71.4% respectively; $p<0.02$). Pathological fractures appeared to influence the femoral lesion adversely. Patients presenting with femoral fractures had a statistically inferior survival to patients with femoral lesions who entered preoperative chemotherapy with intact femurs (40.0% vs. 82.8%; $p<0.05$ Chi square).

Limb-preserved patients had superior gait and energy characteristics to these patients undergoing comparable level amputation. Conversely, en bloc procedures had a nine-fold higher, combined acute and late complication rate as compared to amputation. Skin necrosis has been lately almost eliminated by utilizing fluorescein intraoperatively to determine potentially devitalized wound flaps. Prosthetic breakage has been prevented by employing semiconstrained titanium devices. Loosening remains a problem hopefully amenable to porous ingrowth fixation. Efforts at improved reconstruction are only meaningful in the setting of properly chosen and executed en bloc procedures. The high level of patient survival and low recurrence rate occurs only when limb preservation is offered only to patients with a free neurovascular bundle, potential preservation of a normal cuff of tissue, attainment of growth maturity, reasonable tumor size, a reliable patient, an absence of infected biopsy site, and absence of a pathological fracture. Even at Memorial Hospital, where limb preservation is a desired procedure, most patients still undergo amputations.

REFERENCES

1. Dahlin, D.C. and Coventry, M.B.: Osteosarcoma: A study of 600 cases. *J. Bone Joint Surg. 49A:* 101-10, 1967.
2. Enneking, W.F., Spanier, S.S., and Goodman, M.A.: A system of the surgical staging of musculoskeletal sarcoma. *Clin. Orthop. 153:* 106-20, 1980.
3. Huvos, A.G., Rosen, G., and Marcove, R.C.: Primary osteogenic sarcoma. Pathologic aspects in 20 patients after treatment with chemotherapy, en bloc resection and prosthetic bone replacement. *Arch. Pathol. Lab. Med. 101:* 14-18, 1977.
4. Huvos, A.G.: *Bone Tumors: Diagnosis, Treatment and Prognosis.* Saunders, 1979, pp. 47-93.
5. Lewis, R.J. and Lotz, M.J.: Medullary extension of osteosarcoma. *Cancer 33:* 371-75, 1974.
6. Marcove, R.C., Mike V., Hajek, J.V., et al.: Osteogenic sarcoma under the age of 21. A review of 145 pre-operative cases. *J. Bone Joint Surg.* (Am.) *502:* 411-23, 1970.
7. Marcove, R.C.: En bloc resection for osteogenic sarcoma. *Cancer J. Surg. 20:* 521-28, 1977.
8. Marcove, R.C. and Rosen, G.: En bloc resections for osteogenic sarcoma. *Cancer 45:* 3040-44, 1980.
9. Marcove, R.C.: En bloc resection for osteogenic sarcoma. *Bull. N.Y. Acad. Med. 55:* 744-50, 1979.
10. Pade, G.T., McNeer, G., and Coley, B.L.: Interscapulothoracic amputation for malignant tumors of the upper extremity. A report of 31 consecutive cases. *Surg. Gynecol. Obstet. 74:* 161-75, 1942.
11. Rosen, G., Marcove, R.C., Caparros, R., et al.: Primary osteogenic sarcoma. The rationales for pre-operative chemotherapy and delayed surgery. *Cancer 43:* 2163-77, 1979.
12. Rosen, G., Huvos, A.G., Mosende, C., et al.: Chemotherapy and thorocotomy for metastatic osteogenic sarcoma. A model for chemotherapy and rationale: The timing of the thoracic surgery. *Cancer 41: 841-49, 1978.*
13. Rosen, G., Caparros, B., Huvos, A.G., et al.: Pre-operative chemotherapy for osteogenic sarcoma: Selection of post-operative adjuvant chemotherapy based on the response of the primary tumor to pre-operative chemotherapy. *Cancer 49:* 1221-30, 1982.
14. Sweetman, R.: Amputation in osteosarcoma. *J. Bone Joint Surg. 55B:* 189-92, 1973.
15. Van Ness, C.P.: Rotationplasty in the treatment of congenital defects of the femur. *J. Bone Joint Surg.* (Br.) *32B:* 12-16 1950.